IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: **Roger Petrus Gerebern Vandecruys**	Confirmation No.: **4563**
Application No.: **10/674,701**	Group Art Unit: **1618**
Filing Date: **September 20, 2003**	Examiner: **Micah Paul Young**

For: **Pregelatinized Starch In A Controlled Release Formulation**

Mail Stop AF
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

PRE-APPEAL BRIEF REQUEST FOR REVIEW

Applicants respectfully request review of the final rejection in the above-identified application. The amendments submitted with the Response filed July 28, 2008 were not entered. This request is being filed with a Notice of Appeal. The review is requested for the reasons stated on the attached sheets.

REMARKS

Claims 20-28, 32, 33, 36, 37, and 39 are pending.

The Claimed Invention

The present invention is directed to hydrophilic, controlled-release tablet formulations for oral ingestion. These tablets comprise, among other things, pregelatinized starch; 9-hydroxyrisperidone, a pharmaceutically acceptable acid addition salt thereof, an N-oxide form thereof, or a stereochemically isomeric form thereof as active ingredient; and one or more viscous hydrophilic polymers. The formulation of these tablets is such that the active ingredient is released *in vivo* in a controlled fashion, preventing dose-dumping, allowing at least a two-fold reduction in dosing frequency, an increase in patient compliance, or an increase in therapeutic performance, as compared to a conventional dosage form. The claimed invention is neither described nor suggested in the prior art.

Rejection under 35 U.S.C. § 103

The claims stand rejected under 35 U.S.C. § 103 as allegedly obvious over Ricky (U.S. 5,792,477), Shimizu (U.S. 5,824,339) and Curatolo (U.S. 5,605,889). The Applicants disagree.

The Office alleges that Rickey describes an oral solid tablet comprising the active agent and polymer of the present claims. This is an incorrect characterization of Rickey. Nowhere in Rickey is an oral formulation described. Rather, Rickey describes the preparation of *depot* formulations for *injection* of microparticles:

> "whereby administration of the microparticles to a patient can be carried out with a *standard gauge needle*. Preferably, the drug-loaded microparticles are dispensed to patients in a single administration, releasing the drug in a constant or pulsed manner into the patient and eliminating the need for repetitive *injections*. . . . Prior to administration to a patient, the dry microparticles can be suspended in an acceptable pharmaceutical liquid vehicle, . . whereupon the suspension is *injected into the body*."

Rickey at col. 17, lines 42-54 (emphasis added). Rickey does not describe solid tablet formulations for oral administration.

Curatolo is also not within the scope of the claimed invention. Curatolo describes formulations of azithromycin that exhibit substantially no adverse food effect. Curatolo at

col. 2, lines 35-38. Curatolo describes formulations do not exhibit a food effect because "they either provide azithromycin ready for dissolution in the GI tract *essentially immediately* following ingestion (suspensions), or they *disintegrate rapidly following ingestion* (tablets) and thereby provide azithromycin rapidly for dissolution." *Id.* at col. 5, lines 6-20 (emphasis added). As such, Curatolo teaches the "dose-dumping" the present invention's controlled release formulation specifically avoids.

Shimazu is also not within the scope of the present invention. Shimazu is directed to the preparation of compositions that effervesce when dispersed in water. The resulting *solution*, not the composition alone, *i.e.*, not the tablet, is then ingested. *See* Shimazu Abstract; *see also,* col. 3, lines 36-37 ("[T]he present invention relates to an effervescent composition."). In addition, 9-hydroxyrisperidone is ***not*** within the list of useful active substances. Shimazu at col. 5, lines 10-58. Moreover, Shimazu only describes "pregelatinized starch" as a binder *potentially* useful for "increas[ing] the strength of the core-shell powders" (Shimazu at col. 6, lines 36-46) and as *potentially* useful as a core component (*Id.* at col.4 , line 17). Pregelatinized starch is noticeably absent from any of the working examples.

The cited art is directed to pharmaceutical formulations outside the scope of the present invention. Rickey is directed to injectable formulations; Curatolo is directed to rapid dissolution formulations; and Shimazu is directed to effervescent tablets for dissolution in aqueous solution prior to ingestion. In contrast, the present invention is directed to controlled-release tablets for oral ingestion. Thus, the cited art, either alone, or in any acceptable combination, fails to teach or suggest any limitation of the claimed invention. A *prima facie* case of obviousness has not been established. Withdrawal of the rejection is respectfully requested.

The Applicants assert that claims 20-28, 32, 33, 36, 37, and 39 are in condition for allowance. An early Notice to that effect is respectfully solicited.

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